

### **III. REMARKS**

#### **A. Status of the Claims**

Claims 6-7, 13-16, 21 and 24 are currently pending. Claims 1-5, 9-12, 17-20 and 22-23 have been cancelled without prejudice. Claims 6, 7, 9, 21 and 24 have been amended without prejudice. Support for these amendments can be found throughout the application as originally filed, e.g., in the originally filed claims and Example 5. Applicants respectfully submit that no new matter has been added by virtue of this amendment.

#### **B. Claim rejection under 35 U.S.C. §103**

##### **1. Goldie et al.**

In the Office Action, the Examiner rejected claims 6-8, 13-16, 20-21 and 24 under 35 U.S.C. § 103(a) as being unpatentable over Goldie et al., U.S. 4,844,909 (hereinafter "the Goldie reference).

This rejection is respectfully traversed. Applicants submit that the Goldie reference, at the very least, fails to teach or suggest a dosage form that provides blood levels of hydromorphone over 500 pg/ml at 12 hours after administration to a human patient, and at least about 300 pg/ml at 24 hours after administration to human patients, as recited in the present claims.

In support of this position, the Examiner's attention is directed to Tables 5 and 6 of the Goldie reference, which shows the following mean plasma concentrations at 12 and 24 hours:

<u>Table 5</u>	
12 hours	1.0 ng/ml <sup>-1</sup>
24 hours	1.1 ng/ml <sup>-1</sup>

<u>Table 6</u>	
12 hours	2.1 ng/ml <sup>-1</sup>
24 hours	1.4 ng/ml <sup>-1</sup>

Applicants note that Table 6 lists the plasma concentration as "ng/ml", however it appears that this is a typographical error as all other occurrences of plasma concentrations in the reference (e.g., Table 5 and column 1, lines 65-68) indicate that plasma levels that are measured in  $\text{ng/ml}^{-1}$ .

As can be appreciated by one skilled in the art, the mean blood level of hydromorphone in pg/ml can be calculated from the  $\text{ng/ml}^{-1}$  value provided in the Goldie reference to provide the following values in Tables 5 and 6:

<u>Table 5</u>		<u>Table 6</u>	
12 hours	$1.0 \text{ ng/ml}^{-1} = 100 \text{ pg/ml}$	12 hours	$2.1 \text{ ng/ml}^{-1} = 210 \text{ pg/ml}$
24 hours	$1.1 \text{ ng/ml}^{-1} = 110 \text{ pg/ml}$	24 hours	$1.4 \text{ ng/ml}^{-1} = 140 \text{ pg/ml}$

As can be gleaned from this data, the presently claimed plasma concentrations at 12 and 24 hours are significantly higher than the plasma concentrations of the Goldie formulations. For example, the presently claimed hydromorphone mean blood level at 12 hours is 500 pg/ml, in contrast to the values calculated from the Goldie reference of 100 pg/ml and 210 pg/ml at 12 hours. Further, the presently claimed hydromorphone mean blood level at 24 hours is 300 pg/ml, in contrast to the values calculated from the Goldie reference of 110 pg/ml and 140 pg/ml at 24 hours.

Accordingly, it is respectfully submitted that the Goldie reference does not teach or suggest a dosage form that provides mean blood levels of hydromorphone over 500 pg/ml at 12 hours after administration to human patients, and at least about 300 pg/ml at 24 hours after administration to human patients, as recited in the present claims.

In view of the above, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) over Goldie et al. be removed.

**2. Goldie et al. in view of Oshlack et al.**

In the Office Action, the Examiner further rejected claims 9-10 and 22-23 under 35 U.S.C. § 103(a) as being unpatentable over Goldie et al. in view of Oshlack et al., U.S. 5,286,493.

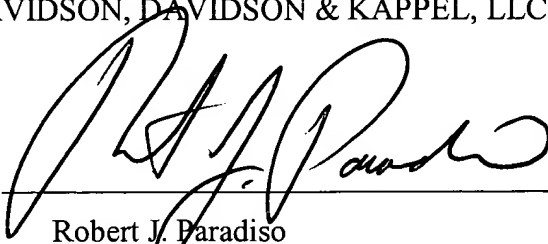
As claims 9-10 and 22-23 have been cancelled, this rejection is now moot. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) over Goldie et al. in view of Oshlack et al. be removed.

**IV. CONCLUSION**

In view of the amendments made and arguments presented, it is respectfully requested that the Examiner's rejections be withdrawn. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application. An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,

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